The Examiner withdrew claims 33-34 as drawn to a non-elected invention, and claims 12, 14, 38 and 39 were also withdrawn as they are drawn to a non-elected species. Applicant has cancelled claims 7-9, 12-14, and 21-34, reserving the right to prosecute that subject matter, as well as the originally presented claims, in continuation applications. As such, claims 1-6, 10-11, 13, 15-20 and 35-39 are in the case. Claims 1-6, 10-11, 13, 15-20 and 35-37 are under examination.

Claim Objections

The Examiner objected to claims 7, 21, 26, 27, 29 and 32 because of the term "CIITA" appearing therein. Applicant has amended the claims to replace this term with its meaning from the specification, *i.e.*, "Class II transactivator" – *see, e.g.*, Applicant's specification at page 4, line(s) 10-11.

Double Patenting

Rejection of Claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §101

The Examiner provisionally rejected Claims 1-8, 10, 11, 13, 15-20 and 35-37 under 35 U.S.C. §101 as claiming the same invention as claims 1-7, 9-11, 13-16, 18, 20-26 and 31-33 of copending U.S. Application No. 09/960,471. Since Applicant has amended the claims herein, the rejection is believed to be moot and withdrawal is therefore proper.

The Examiner provisionally rejected Claims 2-8, 10-11, 13, 15-20 and 35-37 under 35 U.S.C. §101 as claiming the same invention as claims 2-7, 9-11, 13-16, 18, 20-26 and 31-33 of copending U.S. Application Nos. 10/056,608, 10/056,288, 10/056,645, 10/056,133 and 10/056,606. The Examiner also provisionally rejected Claims 1-8, 10-11, 13, 15-20 and 35-37 under 35 U.S.C. §101 as claiming the same invention as claims 1-7, 9-11, 13-16, 18, 20-26 and 31-33 of copending U.S. Application No. 10/056,646. Applicant respectfully points out that the claims of those cited applications have already been cancelled by amendment. This rejection is moot.

Obviousness-Type Double Patenting

Rejection of Claims 1-11, 13, 15-32 and 35-37

The Examiner rejected claims 1-11, 13, 15-32 and 35-37 under the judicially-created doctrine of obviousness-type double patenting over claims 36-48 and 76-93 of copending U.S. Application Nos. 10/056,608, 10/056,288, 10/056,645, 10/056,133 and 10/056,606. The Examiner also rejected claims 1-11, 13, 15-32 and 35-37 under the judicially-created doctrine of obviousness-type double patenting over claims 36-48 and 76-93 of copending U.S. Application Nos. 10/056,646. Applicant respectfully points out that the claims of those cited applications have already been cancelled by amendment. This rejection is moot.

Written Description

Rejection of Claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §112, first paragraph. The specification was said to fail to adequately teach how to make and/or use the claimed invention and therefore fail to provide an enabling disclosure. In particular, the Examiner stated that the specification fails to set forth the criteria that defines a "functionally equivalent molecule of a statin." Applicant traverses in view of the amendments made herein.

Without agreeing to the propriety of the rejection, and to place the case in better condition for allowance, Applicant has amended the claims to particularly recite a group of well-known statins that are fully described in Applicant's specification, namely, compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and simvastatin. The claims are fully enabled by Applicant's specification; *see, e.g.,* Applicant's specification at page 6, lines 12-25.

In view of the amendments presented herein, the rejected claims are submitted to be patentable under 35 U.S.C. §112, first paragraph, and withdrawal of the rejection is in order and is respectfully requested.

Rejection of Claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter Applicant regards as his invention. Applicant traverses in view of with the following comments.

Without agreeing to the propriety of the rejection, and to place the case in better condition for allowance, Applicant has amended the claims as follows. The term "mammal in need of such treatment" has been amended to more particularly point out the claimed patient population, *i.e.,* mammals with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression. The claims have been amended, to clarify the statin family, to particularly recite a group of statins which fall within Applicant's description of "statin" in his specification, *see, e.g.,* page 6, lines 12-25. Lastly, claims 21 and 26 have been cancelled, mooting the objections recited in the Office Action to terms recited in those claims.

In view of the amendments presented herein, the rejected claims are submitted to be patentable under 35 U.S.C. §112, second paragraph, and withdrawal of the rejection is in order and is respectfully requested.

Novelty

Rejection of Claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §102(e)

The Examiner rejected claims 1-11, 13, 15-32 and 35-37 under 35 U.S.C. §102(e) as anticipated by Partridge U.S. Patent No. 6,403,637 B1 ("Partridge").

Applicant traverses, since the presently amended claims have an invention date prior to the filing date of Partridge, *i.e.,* the 35 U.S.C. §102(e) date, as stated in the Declaration of Francois Mach submitted herewith.

Even if Partridge were available as prior art (which it is not), Partridge would not anticipate the pending claims.

Partridge was cited for teaching treatment of arthritis by administering an effective amount of atorvastatin to a mammal, *e.g.,* claims 1-13. The Examiner argued that Partridge anticipates the claimed invention inherently. The taught administration of atorvastatin for treating arthritis was argued to inherently provide a protective utility, *i.e.,* to achieve MHC Class II immunomodulation. Since the claims were not considered to "distance [them] from the anticipated prophylactic utility," the claims were deemed to be anticipated by "the prior inherent use."

Partridge does not teach administration to the relevant patient population that Applicant's amended claims recite, and therefore the Partridge teaching cannot be a "prior inherent use." Partridge does not anticipate the claimed invention. Partridge describes administering a statin to treat conditions (*i.e.,* osteoarthritis) characterized by cells having excessive amounts of matrix metalloproteinases, *i.e.,* they are aberrant cells compared to normal subjects. In other words, Partridge does not teach administration to the same patient population as Applicant's invention does. It is not at all apparent that the protective effect urged by the Examiner (*e.g.,* achieving MHC Class II immunomodulation) in the presently claimed subjects would even be (or is) achieved in the Partridge subjects. The subjects Partridge treats are therefore not the same patient population as the patient population for which Applicant's invention is useful. Since the respective populations are not the same, the present invention is not anticipated, explicitly or inherently.

Applicant's claims recite achieving MHC-class II-mediated immunomodulation in mammals (*e.g.,* humans) having an *MHC-Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression* by administering a statin to achieve the desired effect (*e.g.,* immumodulation, immunosuppression and/or anti-inflammatory effect.) The invention is useful in treating or preventing conditions where aberrant expression of MHC-class II and/or aberrant activation of CD4 T lymphocytes are implicated, *e.g.,* organ transplantation, autoimmune conditions including Type I diabetes,

multiple sclerosis, rheumatoid arthritis, and psoriasis and chronic inflammatory diseases like atherosclerosis.

Partridge teaches treatment of subjects having conditions characterized by excessive amounts of matrix metalloproteinases like collagenase-3. In point of fact, the invention is directed to treating cells containing *excessive amounts* of matrix metalloproteinases (*see, e.g.,* claim 1) such that inactivation, endocytosis and degradation of the enzyme takes place. Partridge theorizes that matrix metalloproteinases mediate disorders like osteoarthritis, osteoporosis, and breast cancer. One of ordinary skill in the art will recognize these disorders are significantly different from the disorders sought to be treated by the present invention, *i.e.,* where aberrant expression of MHC-class II and/or aberrant activation of CD4 T lymphocytes are implicated, *e.g.,* autoimmune conditions. And, the disorders treated by the instant claims are not characterized by excessive matrix metalloproteinase production.

Further, the Examiner cited Partridge solely for its teaching that a statin, *e.g.,* atorvastatin, could be used to treat arthritis, and points to the mention by Partridge to rheumatoid arthritis at column 6, line 20. This is the only mention of rheumatoid arthritis in the entire patent. The real focus of the patent, however, is osteoarthritis, which is recited about thirty times and is the subject of patent claims and actual test data.

Osteoarthritis and rheumatoid arthritis differ in many ways. There are over one hundred types of arthritis (source: the Arthritis Foundation, copy attached as Appendix B), each with its own indications and root causes. Each are classified as an arthritis, but it is incorrect to state that treatment (or prevention) of one type of arthritis will work for another type. The mere mention of a condition as treatable does not necessarily make it so, as one of ordinary skill in the art clearly recognizes. Rheumatoid arthritis is an immune disorder characterized by inflammation of the synovium, resulting in joint pain, swelling and stiffness. In contrast, osteoarthritis is a degenerative condition. Secondly, unlike osteoarthritis, rheumatoid arthritis is not characterized by cells having excessive amounts of matrix metalloproteinases. (And, given the single mention of rheumatoid arthritis in the entire patent, Partridge's "teaching" of treating rheumatoid arthritis cannot fairly be described as an enabling disclosure.)

That said, the reference cannot fairly said to anticipate the presently claimed invention. The rejection should be withdrawn.

Obviousness

Rejection of Claims 4, 5, 8-10, 16-19 and 35-37 under 35 U.S.C. §103(a)

The Examiner rejected claims 4, 5, 8-10, 16-19 and 35-37 under 35 U.S.C. §103(a) as obvious over Partridge. Note that claims 8 and 9 are cancelled herein, so the rejection is moot to those claims.

Applicant traverses, since the presently amended claims have an invention date prior to the filing date of Partridge, *i.e.*, the 35 U.S.C. §102(e) date. Partridge is not available as prior art. The obviousness rejection should therefore be withdrawn.

Even if Partridge were available as prior art (it is not), Partridge would not render the pending claims obvious. The Examiner concedes that:

- Partridge does not teach mammals not suffering from hypercholesterolemia;
- Partridge does not teach mammals being prepared for organ transplantation;
- Partridge does not teach the dosage ranges of 10-80 or 20-40 mg/day; or the claimed methods of administration.

Nonetheless, the Examiner still argued that since Partridge teaches administering atorvastatin to a mammal, the invention is still obvious.

For the same reasons described above, Partridge does not make the pending claims obvious. The claims describe achieving MHC-class II mediated immunomodulation in mammals (*e.g.*, humans) with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression by administering a statin to achieve the desired effect (*e.g.*, immumodulation, immunosuppression and/or anti-inflammatory effect.) Partridge does not teach or suggest this – it refers only to treatment of subjects having conditions characterized by excessive amounts of matrix metalloproteinases like collagenase-3, and in fact, in cells containing excessive amounts of matrix metalloproteinases (*see, e.g.*, claim 1.)

As noted above, Partridge describes administering a statin to treat conditions (*i.e.*, osteoarthritis) characterized by cells having excessive amounts of matrix metalloproteinases, *i.e.*, in aberrant cells compared to normal subjects. The diseases in the present application are not characterized by matrix metalloproteinase overproduction. Partridge therefore does not teach administration to the same patient population as in Applicant's invention. One of ordinary skill in the art would understand that the 'protective effect' proposed by the Examiner (*e.g.*, achieving MHC Class II immunomodulation) in Applicant's presently claimed subjects could or would be achieved in the Partridge subjects. One of ordinary skill in the art would therefore **not** read Partridge in the way urged by the Examiner and would not find the claimed invention obvious.

Partridge's subjects are not the same patient population as in Applicant's invention. Furthermore, rheumatoid arthritis, as noted above, is clinically and biochemically a very different condition from osteoarthritis, despite the assertion in the Office Action. Patients suffering from rheumatoid arthritis are not expected to have excessive amounts of matrix metalloproteinases. Thus, the subjects Partridge treats do not suffer from conditions like those

taught in Applicant's specification, and in fact are not the same kind of patients. Any comparison between the Partridge and Applicant's invention must therefore, respectfully, fail. Because of all of this, the teachings of Partridge do not fairly suggest the claimed invention, and the rejection respectfully should be withdrawn.

SUMMARY

On the basis of the foregoing amendments, Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact either of the undersigned at the telephone number provided below.

Respectfully submitted,

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Appendix A: marked up version of the claims showing the changes made

In the Claims:

Please cancel claims 7-9, 12-14, and 21-34 without prejudice or disclaimer.

Please amend the claims as follows:

1. (amended once) A method to achieve MHC-class II mediated immunomodulation in a mammal ~~in need of such treatment~~with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression, ~~, which comprises~~ the method comprising administering to ~~the~~ said mammal at least one statin selected from the group consisting of compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and simvastatin, ~~, or a functionally or structurally equivalent molecule,~~ in an amount effective to modulate MHC class II expression in ~~the~~ said mammal.

2. (amended once) A method to achieve MHC-class II mediated immunosuppression in a mammal with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression~~in need of such treatment~~, ~~which comprises~~ the method comprising administering to the mammal at least one statin~~, or a functionally or structurally equivalent molecule~~ selected from the group consisting of compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and simvastatin, in an amount effective to suppress MHC class II expression in ~~the~~ said mammal.

3. (amended once) A method to achieve MHC-class II mediated anti-inflammatory effect in a mammal with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression~~in need of such treatment~~, ~~which comprises~~ the method comprising administering to ~~the~~ said mammal at least one statin~~, or a functionally or structurally equivalent molecule~~ selected from the group consisting of compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and simvastatin, in an amount effective to suppress MHC class II expression in ~~the~~ said mammal.

15. (amended once) The method of claims 1, 2 or 3, wherein ~~the~~ said statin~~, or a functionally or structurally equivalent molecule,~~ is administered in the absence of any other immunosuppressive agents.

16. (amended once) The method of claims 1, 2 or 3, wherein said amount is ~~comprised~~ between 10 and 80 mg per day.

17. (amended once) The method of claims 1, 2 or 3, wherein said amount is ~~comprised~~ between 20 and 40 mg per day.

35. (amended once) A method of treating a patient afflicted with an autoimmune disease characterized by IFN-γ inducible Class II transactivator expression, comprising administering to said patient a compound that inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA reductase) in an amount effective to treat said disease.

37. (amended once) A method of treating a patient suffering from an autoimmune disease or condition characterized by IFN-γ inducible Class II transactivator expression comprising:

    - administering to said patient at least one compound, capable of measurable HMG-CoA reductase inhibition and inhibition of MHC Class II expression in said patient, in an amount effective to treat such autoimmune disease or condition.